Plasticity of visual field representations

De Oliveira Carvalho, Joana

DOI:
10.33612/diss.128352681

CHAPTER 7

Discussion

7.1 General Discussion

The general focus of this thesis is on understanding how the organization of the visual cortex is shaped by visual experience, predictive mechanisms, damage due to visual field defects or developmental disorders. More specifically, I combined neuroimaging techniques such as fMRI with biologically driven neurocomputational models to investigate whether neurons – at a population or subpopulation level – have the capability to modify their receptive field properties following damage (artificial and natural) to the human visual system or following changes in the stimulus. In the following section, I briefly describe the main findings of the chapters in the thesis and discuss their significance and implications.

7.1.1 The recruitment of neural resources in a cortical region depends on the stimulus and task

Using a second-order retinotopic stimulus, we showed that the estimated pRF properties change significantly when compared with a standard luminance contrast stimulus. The latter affected a wide range of neuronal subpopulations, while our second-order stimulus only affected a subset of those neurons – i.e. those that are sensitive to orientation contrast. By combining our results with those from previous studies (Le et al., 2017), it now seems plausible to assume that 1) the recruitment of neural resources in a cortical region depends on the stimulus and task; 2) ventral cortical areas may contain different overlapping representations of the visual field and 3) parvocellular neurons (stimulated by spatial frequency/words/orientation) and magnocellular neurons (luminance) may have overlapping cortical maps in a single area. These findings have powerful implications regarding the use of pRF mapping to measure the organization of the visual cortex; this shows that the pRF properties in healthy observers are not stable and depend on the stimulus, task and environmental factors. This constrains the straightforward assessment of neuroplasticity, as it is essential to separate the effects of stimulus properties from cortical reorganization in visual system pathologies.

7.1.2 Micro-probing enables detailed characterization of the structure and function of the visual cortex.

To overcome many of the limitations of the current the pRF modeling approaches, we developed a new visual field mapping approach, which we call micro-probing (MP). This approach enhances spatial resolution and simultaneously enables the identification of unexpected RF shapes and subpopulations. This boosts the understanding of the visual cortex as it allows fine-grained characterization of the visual areas (multiple subpopulations and its heterogeneous shape) and enables us to map – without any specific prior assumptions – unexpected RF shapes such as the bilateral receptive fields symmetrical to the vertical meridian, which are a characteristic of albinism. Additionally MP results in visualization of the data underlying any pRF estimates. This is extremely useful for reconstructing the visual field (see next section), for meticulous data cleaning and for determining the misrouted cortical zone. Therefore we advocate the use of MP when the study outcomes are unpredictable or may rely on aggregate characteristics of RFs. In particular, this would apply to studies on: 1) neurodevelopment and neuroplasticity, 2) ophthalmic and neurological pathologies, and 3) cognitive effects. We conclude that MP provides a versatile and powerful high-resolution approach to reveal the functional properties of the brain, which is essential for linking its function to behavior and for understanding its plasticity.

7.1.3 Predictive masking results from a system-wide reorganization of the neural populations, which is guided by extrastriate cortex.

Seeing involves more than the light that enters our eyes. A remarkable example is the capability of the visual system to fill in missing information. In response to introducing an artificial scotoma into the visual field, pRFs shifted their preferred position towards the AS border. Moreover, extrastriate areas reweighted their sampling of area V1 towards information from outside the AS projection zone. Such a reweighting enables the neurons within the scotoma projection zone to gather information from spared sections of the visual field (Baker et al., 2005; Dilks et al., 2009; Gilbert and Wiesel, 1992; Pettet and Gilbert, 1992; Schumacher et al., 2008) which results in the masking of the scotoma with the most likely information. Our findings suggest that a system-wide reconfiguration of neural populations in response to a change in visual input is guided by extrastriate signals and underlies the predictive spatial masking of scotomas.

These findings have important implications in the context of vision restoration therapies. First, similar predictive masking mechanisms are thought to be present in natural visual field defects, in particular those affecting the periphery, such as glaucoma. Second, therapies focused on higher cognitive processes, such as attention-based training, might improve visual perception by reallocating scarce neuronal resources to the intact sections of the visual field (Dundon et al., 2015).

7.1.4 Visual field reconstruction using fMRI-based techniques enables the evaluation of vision loss, and may complement ophthalmologic tests to clinically assess visual field defects

To understand the extent of visual damage, measuring the visual field is crucial. The standard method to measure the visual field is standard automated perimetry (SAP). However, these tests are highly sensitive to attention and experience of the subject. Using micro-probing, the visual field at various levels of cortical visual processing was reconstructed. Using simulated and natural visual field defects, we determined the degree of similarity between the visual field coverage map and the perimetric outcomes. We found that both MP and the conventional pRF-based visual field reconstruction resulted in accurate measures of the visual function given that we could detect the simulated visual field defects. Applied to natural visual field defects of participants with glaucoma, overall the fMRI-based visual field reconstruction techniques could detect the VFD also detected by SAP. In particular, our new approach (MP) could better predict the SAP contrast sensitivity than the conventional pRF mapping technique could. However, for some of the participants with glaucoma, there was a dissociation between the fMRI-based reconstructed visual field and the visual field assessed using SAP. This suggests the following: 1) the methodological differences between SAP and fMRI-based VF mapping techniques result in an assessment of distinctive aspects of the VF, 2) that glaucoma patients might be able to fill in the visual field defects and thus elicit fMRI activity in part of their scotoma projection zone and 3) that the combination of fMRI and neurocomputational models results in an objective and feasible method that may complement current ophthalmic evaluations. This is particularly important when evaluating the impact of vision restoration and rehabilitation therapies on visual processing beyond the retina in the brain (Silson et al., 2018). Therefore, the use of retinotopic mapping, in particular MP, reveals important characteristics of the functioning of the visual system that cannot be assessed with standard ophthalmic examinations.

7.1.5 Cortical plasticity requires that stimulus-driven approaches are complemented by cortical circuitry models

We have shown that the pRF properties in the adult visual cortex are malleable in health and disease. However, increasing evidence indicates that variations in pRFs can be driven by three aspects: methodological biases associated with conventional pRF mapping, the effect of stimulus and task and the physiological mechanisms of attention control and surround suppression (Binda et al., 2013; Klein et al., 2014; Le et al., 2017; Yildirim et al., 2018). Therefore we argue that the inherent reliance of these approaches on visual input is still a major challenge for interpreting results in terms of neuroplasticity in such disorders. In our view, this calls for rethinking the current approaches to studying cortical neuroplasticity. We suggest that methods that do not require visual stimulation at all, such as Cortico-Cortical Modeling, are very appropriate for assessing visual cortical reorganization. Such approaches may avoid many of the complications associated with the stimulus-driven pRF methods.

7.2 Clinical applications

7.2.1 Functional MRI as clinical tool to access the cortical plasticity of the visual cortex

A fundamental question in visual neuroscience is the degree to which the adult visual cortex has the capability to adapt its function and structure. Understanding the neuroplasticity of the visual cortex is becoming particularly relevant in the context of vision restoration: bringing back (partial) vision to people who have become blind due to ophthalmic disorders such as glaucoma, aged-related macular degeneration, or retinitis pigmentosa. With recent developments in technology and medical practice, vision restoration is now more feasible than ever due to retinal and cortical implants, gene therapy, and stem cell therapy. To safeguard the success of such new therapies, deep understanding of neuroplasticity is essential. Two aspects are particularly critical: 1) whether the visual cortex retains the ability to process visual information following long-term blindness, and 2) whether neurons and their cortical networks reorganize following the restoration of visual function. Non-invasive neuroimaging techniques together with neural models have the potential to answer these fundamental questions and to identify neurodegenerative centers in the visual cortex. In this thesis we found compelling evidence on the following aspects pertaining to plasticity:

-Congenital visual pathway disorders such as albinism result in highly atypical RF profiles. In albinism, each hemisphere has a complete representation of the entire visual field. Our research has provided tools to quantify the degree of misrouting and the misrouting projection zone.

-In healthy observers, the predictive masking of simulated scotomas is associated with changes in receptive field properties and with the sampling of the scotomatic region. This reconfiguration is most likely driven by signals from higher order areas. Although predictive masking impairs the early detection of disease, it is an important mechanism that ensures the stability of perception.

However, there are several factors that need to be taken into account when interpreting these findings. First, the techniques that we used reflect the aggregate RF properties at the population and/or subpopulation level. The receptive field dynamics that we measured can result from changes in a subset of neurons (Haak et al., 2012). Second, evaluating neuroplasticity requires complex and accurately controlled experimental conditions (e.g. for artificial scotomas and visual acuity). Third, ectopic receptive fields may result from extra-classical RF modulations and from attentional modulation. Fourth, the factors that influence the degree to which the visual cortex can reorganize – such as damage to the RCG, extent of the disease, and onset and duration of the disease – still have to be determined.

7.2.2 Functional MRI as a clinical tool to detect and monitor damage to the visual system

Functional MRI, together with advanced RF mapping techniques such as MP, are feasible approaches for assessing damage to the visual field, at different levels of cortical visual processing. Such approaches are very relevant to diseases in which perception is dissociated with the damage to the visual pathway, such as glaucoma and diabetic retinopathy. In such cases fMRI-based approaches have the capability to detect perceptual masking mechanism, e.g detecting the VFD at V1 but not at higher order areas. Additionally, fMRI-based can provide VF information in patients unable to perform SAP because of mental or physical limitations. Moreover, emerging therapeutic interventions, such as retinal ganglion cell transplantation and retinal or cortical implants, require tools that support the diagnosis and monitoring of the disease throughout the visual pathway (Mathieson et al., 2012; Venugopalan et al., 2016).

7.3 Future directions in research

This thesis comprises several studies that point to functional changes in the reorganization of the brain in healthy and diseased visual systems. Although these changes can be interpreted as a manifestation of neuronal plasticity, the underlying mechanisms are still not clear. In particular, little is known about the mechanisms that can trigger functional reorganization and about the role of intracortical feedback from higher visual areas in the early visual cortex. Below, we discuss possible strategies to study this in the future.

7.3.1 High resolution MRI: Column-specific and layer-specific plasticity

The emergence of ultra high field MRI, with field strengths of 7T and above, has been instrumental for studying cortical functioning in detail in humans. Due to its high sensitivity and level of detail, this approach reveals aspects that are generally masked at a coarser scale. Since many neural processes, such as feedforward and feedback signalling, are segregated into distinct cortical layers, imaging the human cortical structure in-vivo at the mesoscale enables differentiation of functional activation across these cortical laminae (Fracasso et al., 2016). This paves the way towards understanding human cortical circuitry and dysfunction. Therefore, it would, for instance, be of interest to repeat the predictive masking study (reported in Chapters 4) using ultra high fields to investigate the origin and the neural substrate of the proposed reorganization. We could also test whether the ability of the visual cortex to reorganize following damage to the visual system is layer-specific.

Moreover, applying MP to ultra-high resolution data will be crucial to disentangle if the multiple neuronal subpopulations of RFs found within a voxel of healthy participants (chapter 3) result from: 1) neurons responding to multiple positions in the visual field, 2) the aggregate response of neurons tuned to different spatial and temporal properties,

or 3) methodological biases, i.e partial voluming and noise in the BOLD signal.

7.3.2 Incorporate and develop cortical circuitry models

An unanswered question is whether the changes in RFs are driven by the unmasking of cortical feedback from extrastriate visual areas and or lateral connections. Cortical circuitry models could be used to answer this question. For instance, connective field modeling (Haak et al., 2013) is a major advance on approaches that rely on visual input, as it emphasizes the spatial profile of the functional connectivity between visual areas and provides insight into the information flow. Moreover, as a stimulus-independent analysis it avoids many of the biases associated with stimulus-driven approaches such as pRF. The use of cortico-cortical models together with high-resolution functional data may enable the study of short-range connections at laminar and columnar levels and their interaction across layers. It would be a tremendous advancement to measure the flow and directionality of information across cortical layers and to disentangle feedback from feedforward.

In this thesis, I proposed two ways to possibly improve cortico-cortical models. The first one is to develop a connective field model based on the micro-probing approach. This could potentially enhance the detail with which we can map the flow of information between brain areas and show if a population of neurons within a voxel perhaps has multiple connective fields. The second one is to incorporate cortico-cortical interactions between the neural population of a particular voxel and its neighbours, into the pRF model (chapter 6). Although this latter approach will still rely on visual stimulation, it may reflect how the activity of one neuronal population of neurons is influenced by that of nearby neighboring populations.

7.3.3 Quantification of the level of brain plasticity in visual processing in disease and following visual restoration

Research on how the visual cortex reorganizes following visual loss has focused primarily on foveal and central visual loss. Given that peripheral and central vision have different roles in perception – e.g. the former provides navigation clues and the latter is involved in detail vision such as e.g. relevant to reading – and that this distinction is encoded in the brain, the neuronal changes following the loss of central or peripheral vision may also differ. Moreover, peripheral visual field defects are more easily masked by predictions based on the surrounding spatial information. Most likely, this results from partial stimulation of the large receptive fields that encode the periphery of the visual field. For these reasons, it would be relevant to measure the possible reorganization mechanisms associated with glaucoma. However, studies of peripheral visual loss are complicated by two factors: 1) the variability in the location and extent of the visual field defect and the uncertainty associated with onset of the disease; and 2) finding adequate control conditions which take into account the differential visual input between participants with glaucoma and control participants. Controlling for these factors, requires to match the visual input of each participant with glaucoma with the respective control, by

simulating the loss in contrast sensitivity in the control participants, this is fundamental to disentangle cortical reorganization from neuronal responses to differential visual input.

Moreover, due to the increasing possibilities offered by vision restoration therapies and recent developments in fMRI-based neural models, we now have the opportunity to study how the brain adapts following vision restoration. This will help to clarify whether plasticity can be reversed, and may be maladaptive; and how vision restoration affects cross-modal plasticity. Such enhanced knowledge of brain-eye interaction may provide insight into pre-treatment and post-treatment strategies to optimize the outcomes of restorative therapies.

7.4 References

Baker, C.I., Peli, E., Knouf, N., Kanwisher, N.G., 2005. Reorganization of visual processing in macular degeneration. J. Neurosci. 25, 614–618.

Binda, P., Thomas, J.M., Boynton, G.M., Fine, I., 2013. Minimizing biases in estimating the reorganization of human visual areas with BOLD retinotopic mapping. J. Vis. 13, 13.

Dilks, D.D., Baker, C.I., Peli, E., Kanwisher, N., 2009. Reorganization of Visual Processing in Macular Degeneration Is Not Specific to the "Preferred Retinal Locus." J. Neurosci. 29, 2768–2773.

Dundon, N.M., Bertini, C., Làdavas, E., Sabel, B.A., Gall, C., 2015. Visual rehabilitation: visual scanning, multisensory stimulation and vision restoration trainings. Front. Behav. Neurosci. 9, 192.

Fracasso, A., Petridou, N., Dumoulin, S.O., 2016. Systematic variation of population receptive field properties across cortical depth in human visual cortex. Neuroimage 139, 427–438.

Gilbert, C.D., Wiesel, T.N., 1992. Receptive field dynamics in adult primary visual cortex. Nature.356, 150-2.

Haak, K.V., Cornelissen, F.W., Morland, A.B., 2012. Population receptive field dynamics in human visual cortex. PLoS One 7, e37686.

Haak, K.V., Winawer, J., Harvey, B.M., Renken, R., Dumoulin, S.O., Wandell, B.A., Cornelissen, F.W., 2013. Connective field modeling. Neuroimage 66, 376–384.

Le, R., Witthoft, N., Ben-Shachar, M., Wandell, B., 2017. The field of view available to the ventral occipito-temporal reading circuitry. J. Vis. 17, 6.

Klein, B.P., Harvey, B.M., Dumoulin, S.O., 2014. Attraction of position preference by spatial attention throughout human visual cortex. Neuron 84, 227–237.

Mathieson, K., Loudin, J., Goetz, G., Huie, P., Wang, L., Kamins, T.I., Galambos, L., Smith, R., Harris, J.S., Sher, A., Palanker, D., 2012. Photovoltaic Retinal Prosthesis with High Pixel Density. Nat. Photonics 6, 391–397.

Pettet, M.W., Gilbert, C.D., 1992. Dynamic changes in receptive-field size in cat primary visual cortex. Proc. Natl. Acad. Sci. U. S. A. 89, 8366–8370.

Schumacher, E.H., Jacko, J.A., Primo, S.A., Main, K.L., Moloney, K.P., Kinzel, E.N., Ginn, J., 2008. Reorganization of visual processing is related to eccentric viewing in patients with macular degeneration. Restor. Neurol. Neurosci. 26, 391–402.

Silson, E.H., Aleman, T.S., Willett, A., Serrano, L.W., Pearson, D.J., Rauschecker, A.M., Maguire, A.M., Baker, C.I., Bennett, J., Ashtari, M., 2018. Comparing Clinical Perimetry and Population Receptive Field Measures in Patients with Choroideremia. Invest. Ophthalmol. Vis. Sci. 59, 3249–3258.

Venugopalan, P., Wang, Y., Nguyen, T., Huang, A., Muller, K.J., Goldberg, J.L., 2016. Transplanted neurons integrate into adult retinas and respond to light. Nat. Commun. 7, 10472.

Yildirim, F., Carvalho, J., Cornelissen, F.W., 2018. A second-order orientation-contrast stimulus for population-receptive-field-based retinotopic mapping. Neuroimage 164, 183–193.